Radiology
December Podcast

Hi everyone. This is Dr. David Bluemke in Madison, Wisconsin. This is the first installment of the December 2018 issue.

Two things to start. First, the cover of the December issue. It may look a little bizarre. It looks like two hands, wrapped in old deteriorated bandages. Unlike our usual cover, the cover this month is not an x-ray or CT scan. It is two photographs of a mummy hand, one photo from the front, the other from the back. The mummy is from a museum in Stockholm, Sweden. Why do we have a mummy on our front cover? More on that in just a moment.

Second. In the December issue I have an editorial about artificial intelligence research in radiology. We are seeing a lot more of this. I'm currently reading a book by a venture capitalist. His name is Kai-Fu Lee. The book title is, "AI Superpowers: China, Silicon Valley, and the New World Order." I just barely started the book, and already, Kai-Fu says that radiologists will be replaced by AI. Kai-Fu Lee has worked for Apple, Microsoft, and Google. He had compensation at Google said to be worth in excess of $10 million dollars. His specialty is AI and works with startup firms, now in China. I'm not sure if Kai-Fu is right or not. But I really wish an AI could automatically measure tumors for me. Or draw cardiac MRI contours around the heart. Oh well. Not there yet, Kai-Fu.

My December editorial is about AI research in radiology. We receive many research papers about new AI reading a CT or an MRI scan. A researcher downloads an AI package, feeds in data, and can suddenly identify chest nodules on a CT scan without a radiologist. But does it work?

We have two problems with many AI research papers. First, the AI computer finds a nodule on the chest. But that is all it was trained for. It misses the pneumothorax. It misses the bilateral humeral neck fractures on the chest x-ray, or the massive axillary adenopathy. Well, eventually we hope to train the AI computers better. But that will take time.

The second problem is more basic – does the AI really work at all to find that chest nodule? If you train it on 0.5 mm slices, but what happens if the slice thickness is 2 mm? If it is trained on a Philips CT, can it find the nodule on the Siemens CT? This is a problem of validation. It is unclear if the AI results generalize.

Many research papers in radiology are about proof of concept. What's that? It means that students in the lab were just trying out some new software. They wanted to find gallstones automatically. Or detect a fracture. Or a nodule. They are still trying to figure out which software to use, how much data is needed to train the computer, and so on. Proof of concept. Training a computer to find a nodule is not very interesting. We had conventional software that did this some time ago. First-year radiology residents are extremely proficient.

Let's compare AI research to hardware research. You buy a new MRI scanner. We publish a paper that shows a 3D gadolinium sequence detects 20% more tumors than a standard T2 sequence. Nice. You try it out on your scanner, and the 3D gad sequence really does seem to work. Others have the same scanner, everyone finds the same advantages for the 3D sequence. You change your practice, and add the 3D sequence to your MRI protocol. The sequence gets validated by the radiology community.

AI is different. The MRI scanner lasts for 7 to 10 years. Prototype AI software may last 7 to 10 days. Often, the only group that has the new AI software is the lab that did the research. The software was fully trained only in her laboratory. How can we verify the results?

This is the validation problem of AI – are the results real, are they helpful? Starting immediately, we will be encouraging researchers to make their AI algorithm available for validation by other researchers. This is done in other fields of science and mathematics. There are websites dedicated to archiving computer algorithms. Let's have radiology algorithms archived on websites as well, to promote validation and better science. And just maybe, excellent software will make it into our reading rooms.

Finally, to finish my story about Kai-Fu Lee. Yes, Kai-Fu was pretty down on radiologists. But the book is about China as an AI superpower. There is one huge advantage we already see in radiology research with AI. In the United States, we have a very fragmented healthcare system.

Your hospital patients are different than mine – we cannot exchange patient data without great difficulty. In Europe and China, that is not the case. As a patient, you are part of the national health care system. In addition, China has huge hospital systems and therefore much more data. The largest hospital in the United States is about 1,000 beds. In China, the largest is about 10,000 beds.

In the U.S., our research studies are often 50 to 100 patients. Studies in China give us patient cohorts of 500 to 5,000. Large numbers are critical for teaching AI computers. They need huge amounts of data. Kai-Fu Lee suggests that China has a huge advantage in terms of data to train computers. The U.S. has 300 million people. China has 1.4 billion people. We have Apple iMessage. They have WeChat. We have Amazon, they have Alibaba. We have strict privacy laws – it's hard to collect and share data. China is more flexible. Medical imaging requires huge amounts of data that could make the AI software much smarter in China more rapidly than in the U.S.

OK, that's enough AI talk. Let's go to our first research topic for December. I want to get back to the mummy hand on our front cover.

Soft-Tissue Imaging in a Human Mummy: Propagation-based Phase-Contrast CT

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Jenny Romell, MSc • William Vågberg, MSc • Mikael Romell, MD • Sofia Häggman, PhD • Salima Ikram, PhD • Hans M. Hertz, PhD

The short title of our first article is, "Soft-Tissue Imaging in a Human Mummy: [Propagation-based] Phase-Contrast CT." The researchers are from Stockholm, Sweden. That's also where the mummy hand is from. So what is this about?

Two interesting topics. First is the mummy hand. It is part number MM 18037, a detached hand from the collection of the Museum of Mediterranean and Near Eastern Antiquities. It was brought to Sweden at the end of the 19th century. The mummy hand belonged to an Egyptian man, dated to about 400 BCE. The skin and fingernails are well preserved. The hand is wrapped in linen.

Second interesting topic: phase-contrast CT. What is this? Probably most have not heard of this technology. But we have seen early publications in this journal dating back to the year 2000. I will give you a crash course in older publications in a few minutes. First, what is phase-contrast CT?

Conventional x-ray relies on absorption of x-rays in the body. Bright areas on an x-ray-like bone have a lot of x-ray absorption. Darker areas like the lung did not absorb the x-rays.

Absorption x-rays were discovered by Roentgen in 1895, Nobel Prize in 1901. Frits Zernike developed phase-contrast imaging with visible light, Nobel Prize in 1953. Phase-contrast light microscopy is commonly used. You have seen those pictures – they look very three-dimensional, beautiful images of cellular structure for example.

But the pioneering work in phase-contrast x-rays were only presented in 1965 at Cornell University – a full 70 years after x-ray discovery. And it took another 30 years – in the mid 1990s, for the first biological application of x-ray phase contrast.

So how does phase-contrast x-ray work. Let me start by asking you a question: what is an x-ray? It's part of the electromagnetic spectrum. But that's not specific enough. We talk about an x-ray photon. Remember I spoke about photon counting CT before – we count each x-ray photon that reaches the detector. They are like particles.

But today we are talking about x-rays acting like waves, rather than particles. Like waves on an ocean. When the waves on an ocean pass from deep water to shallow water on the shore, what happens? The wave length stays the same, but the wave changes speed. Some of the waves may crest together in a constructive interference pattern, making larger group waves.

When x-rays pass through the body, the phase of some of the x-ray waves changes. So where there was a peak in the wave, now there is a trough. The discoveries in this area are how to detect the phase changes. With light microscopes, you can add a glass or plastic lens to change the phase of visible light. But the lenses for visible light do not work for x rays. Those inventions are much more recent.

Several methods are now invented to detect the change in phase of x-rays that occurs after passing through the body. The method in the current article is called propagation phase-contrast CT. This is the simplest method: the x-ray source is placed at a greater distance from the object, allowing more time for the phase difference to accumulate. The x-ray waves pass through the object, the phase changes, and the differences in phase are detected, sort of. Propagation x-ray is simpler, but it really does not detect the phase change: it measures the second derivative of difference in the phase. In English, that means that edges of structures are enhanced. The net effect: soft tissue contrast is about three times greater with phase-contrast CT compared to conventional absorption x-ray.

One example, then a summary of prior publications on the topic: think about imaging a meniscal tear on CT. We cannot do this now, because the soft tissue contrast on CT is poor. Phase contrast CT has the potential to show the meniscal tear, or individual tendons in the knee.

Now let's get up to speed. Five papers on x-ray phase contrast published in *Radiology*.

#1 Published in the year 2000. Pieces of liver cancer tissue were imaged by researchers in Japan. Image quality was limited. The problem – a synchrotron x-ray source was needed. I spoke previously about the Hadron Collider in Cern. The underground circle is 27 miles for the synchrotron. Not very practical for medical imaging.

#2 Also published in 2000. The same research group in Japan and also a synchrotron was required. 50-micron blood vessels in a rat liver were identified. A red blood cell is about 8 microns. Again, I did not find the original images very compelling.

#3 Jump forward to 2014. Two big developments. First, researchers from Germany used a conventional x-ray source. In addition, they implemented phase-contrast x-ray with CT scanning. They imaged a piece of a carotid artery. The images show much better detail than conventional x-ray.

#4 Also in 2014: phase-contrast CT of renal cysts in a phantom model. Saline, blood and serum were easily distinguished.

#5 Last one before the mummy hand: A study out of Switzerland. Ex-vivo human coronary artery plaques were studied. Conventional CT saw nothing. Phase-contrast CT showed remarkable detail of the coronary plaque. Definitely an improvement.

Today's article about the mummy hand. Our authors from Sweden used a simple set-up, and a conventional x-ray source. And now, finally, the images are spectacular. Using x-ray CT to identify individual tendons, skin, nerves, and fingernails with incredible detail.

Why image a mummy hand? Certainly, no medical reason. But it captures our attention. Much more interesting than a cadaver hand, although the results would be similar. And much more interesting than another coronary artery plaque.

What else? I mentioned publications in Germany, Switzerland, Japan, and Sweden. Where is the U.S. in all of this? Key research has taken place at the NIH in Bethesda, Maryland. Dr Han Wen made key discoveries of nanometric phase gratings, and simpler, more practical ways to get phase-contrast images. Where is Dr. Wen working? The radiology-oriented NIH institute is NIBIB. But the research being done by Han Wen is in the National Heart, Lung, and Blood Institute, or NHLBI. The head of research on the NIH campus at NHLBI is Dr. Robert Balaban, who was an early researcher in cardiac MRI. Dr. Balaban has a track record of success and is betting on phase-contrast CT. It would be nice if radiology was betting on this was well.

So that's it. These mummy hands are very compelling, and I hope you have time to look at the phase-contrast CT images online. It's easy to find, since its on the cover of the December issue. One more quick thing: how often have you been asked, what is the next invention in medial imaging? During your lifetime, you saw CT revolutionize the field. Then MRI. Then PET. Now you might have an answer to the question. Maybe the next step in our field is phase-contrast CT.

Lung Adenocarcinoma: CT Features Associated with Spread through Air Spaces

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Seon Kyoung Kim, MD, MS • Tae Jung Kim, MD, PhD • Myung Jin Chung, MD, PhD •
Tae Sung Kim, MD, PhD •Kyung Soo Lee, MD, PhD • Jae Ill Zo, MD, PhD • Young Mog Shim, MD, PhD

The topic of the second article for today may be unfamiliar to you, unless you are a chest imaging expert. It is a little specialized, but we will review this briefly. The title is, "Lung Adenocarcinoma: CT Features Associated with Spread through Air Spaces." The authors are from the radiology department at Samsung Medical Center in Korea.

Background: The somewhat new concept in this article is how lung cancer spreads. We think of lung cancer spreading through lung stroma, the lymphatics, to the pleura. Since 2015 however, the World Health Organization has recognized one more way for lung cancer to spread. Through the air space in the lung itself. Let me explain.

The observation is that separate from the main tumor, pathology may identify clumps of tumor cells beyond the main edge of the tumor. This implies that lung cancer may spread microscopically through the air spaces.

The implications are that one or more tumor cells break off from the original tumor mass, migrate through the air space, attach to lung stroma, and start growing. The concept of cells flying through the air to another spot is controversial. We do not know of a mechanism where flying cells happen. Some think that the pathologists get artifacts after they slice the tissue. Cells get spread around when the tissue is cut. Another possibility is familiar to radiologists: in particular, pathologists use 2D images. They do not usually perform 3D imaging like we do.

The entire point of 3D imaging is that you understand the spatial relationships of various structures to each other. Every radiologist has had the experience of unexpected understanding by using a 3D viewing mode.

What about pathologists? In 2012, pathologists from MGH hospital used a stack of 2D slices of four cases of lung cancer. They traced the lung cancer on adjacent pathology slides, just like radiologists would do. They found little islands of lung cancer on different slices were connected in 3D.

With that background, the conclusion is that pathology understanding of spread through air spaces is incomplete. One possibility is detached cancer cells settling in an adjacent place of lung tissue. Another possibility is incomplete understanding of the pathology.

So, why did the WHO create this classification? The major reason is that patients who show spread through air spaces have a worse outcome. If spread through air spaces is present, limited lung resection would not be performed. The entire lobe would be resected.

But there is a catch 22. At present, spread through air spaces cannot be detected until after surgery is performed. At that time, tissue is examined, and the diagnosis is made. But it is too late, the surgery already occurred.

Now we see the rationale of this CT study. The authors wanted to know: are there some CT features that might be present that are associated with spread through air spaces?

Purpose: to describe features on CT that are associated with pathologic diagnosis of spread through air spaces in adenocarcinoma.

Methods: The authors found a cohort of 92 patients who were path positive for spread through air spaces. They also had twice that number, 192, who did not have this finding on pathology. They compared the CT scan findings of the 2 groups.

Results:

#1: spread through air spaces was not present in any of the ground glass lesions. To me, this was the most important results.

#2: 77% of solid tumors had spread through air spaces. For part solid tumors, if the solid component was less than 40%, then spread through air spaces was likely absent.

#3 and final point: if spread through air spaces was present, there was 2-fold greater likelihood of recurrence within 12 months.

Conclusion: This is the first CT series that tried to look at the relationship between the WHO classification and CT findings. The paper introduces us to a relatively new concept of spread through air spaces. Patients with ground glass nodules did not have this. Patients with a low percentage of solid nodule component did not have this. Patients with pathologic findings of spread through air spaces do worse.

The goal is for CT to accurately predict spread through air spaces before surgery. Right now, CT prediction seems unlikely: pathology looks at individual cells, radiology looks at millions of cells. But high-resolution CT techniques may help. A CT scanner with double spatial resolution will soon be available soon from Canon Medical. Photon counting CT may also help. So we will watch out for developments in these areas.

Evaluation of Ovarian Cancer: Initial Application of Coregistered Photoacoustic Tomography and US

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Sreyankar Nandy, PhD* • Atahar Mostafa, MS* • Ian S. Hagemann, MD, PhD • Matthew A. Powell, MD • Eghbal Amidi, MS • Kathryn Robinson, MD • David G. Mutch, MD • Cary Siegel, MD • Quing Zhu, PhD

The next topic makes 3 out of 3 for new concepts and technologies. The short title is "Evaluation of Photoacoustic Tomography and Ultrasound for Ovarian Cancer." The authors are from Biomed Engineering at Washington University and Mallinckrodt Institute of Radiology, in St. Louis.

The new topic is photoacoustic tomography. What is that? Not so complicated. Two underlying concepts as motivation. #1: tumors have more micro vessels than normal tissue. #2: tumors are usually very metabolically active. They extract more oxygen from blood vessels than normal tissue. How can these features be detected?

I will abbreviate photoacoustic tomography as P-A-T, or PAT. In PAT, a laser light is directed into the tissue. Some of the laser light is converted into heat. The heat causes waves that can be detected with ultrasound. The amount of signal is proportional to how much laser light is absorbed by the tissue.

One more feature of the laser: if different laser wavelengths are used, then differences in oxygen content of the tissue can be determined. Oxygen saturation can be determined. Malignant tissue should have lower oxygen saturation than normal tissue.

PAT is experimental. Last year at the RSNA, a multi-center trial was conducted for breast cancer. Results were promising. Malignant tumors had more vessel density and lower oxygen content.

I think of PAT as a potential add-on to ultrasound. Already we have doppler and 3D ultrasound. Maybe PAT could give us another signal that could help determine benign from malignant.

That's the background. In the current study, the authors applied PAT and ultrasound to evaluate ovarian cancer. Ovarian cancer is poorly detected. On MRI, you are likely to consider any cystic lesion in a post-menopausal woman as cancer until proven otherwise. MRI and ultrasound both have low specificity to define the presence or absence of ovarian cancer.

Purpose: The purpose of this study was to evaluate PAT together with ultrasound for evaluation of ovarian cancer.

Methods: This was the first in human application of PAT for ovarian cancer. The authors evaluated 16 patients. 5 had invasive cancers. 10 had benign ovaries or other benign ovarian lesions.

Results:

#1: Total hemoglobin concentration was two times greater in ovarian cancers compared to benign lesions.

#2: Oxygen saturation of malignant lesions was 8% lower than that of benign lesions of the ovary.

Conclusion: This first-of-its-kind study aimed to help a problem that exists. We do not have a good way to predict if an ovarian mass is benign or malignant. Probably the most important factor is simply menopausal status. If there is a cystic lesion in a pre-menopausal patient, its likely benign. In a post-menopausal patient, we assume it could be malignant. That is not so sophisticated. Then we use other criteria like size and septations and nodular features.

The current study is very early, proof of concept. There are some problems with PAT. The most important is that the laser must be within 5 cm of the lesion that is evaluated. The penetration of the laser beam is limited. Perhaps this could be optimized with different wave lengths. Also, in pre-menopausal women, ovarian blood flow is quite high. The method is more likely to be useful in post-menopausal patients. The imaging is slow right now. Probably that could be resolved. All of these new methods are slow when first started.

Photoacoustic tomography is going to be applied to a number of tumor types. I mentioned the breast cancer study that was already completed. Other possible applications are prostate cancer, thyroid, and skin cancer. The technique makes physiological sense. Let's watch this technology to see where it goes.

Overnight Resident versus 24-hour Attending Radiologist Coverage in Academic Medical Centers

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Michael A. Bruno, MD, MS • James R. Duncan, MD, PhD • Andrew J. Bierhals, MD • Rafel Tappouni, MD

Those last topics were complex. Now a topic all radiologists know about. The title is, "Overnight Resident versus 24-hour Attending Radiologist Coverage in Academic Medical Centers." The first author is Michael Bruno. Dr. Bruno is from Hershey Medical Center at Penn State. Co-authors of this opinion piece are from Mallinckrodt and Wake Forest.

The topic is medical education. How do we make the best doctors? A small aside on this topic. Two months ago, I visited Wake Forest Medical School. Wake decided to build the doctor of the future. Besides the obligatory coffee shops, free scooters, and bikes throughout the medical training complex, they are also state-of-the-art in education. They train medical students like we operate MRI scanners. Technologists in a control room adjust and program computer models to simulate every conceivable medical complication. In the adjacent room, individual medical students or groups of students experience simulated patient medical complications. The simulation rooms are filled with cameras observing the medical students from every possible angle. For poor student performance, a teacher moves in when the live video shows the student is stuck. This is modern training for modern students. Most older physicians would feel creepy about 6 or 8 cameras peering at them. But in modern training, this is normal. Students are connected, observed, measured, and trained.

Back to the main topic -- the best training for radiology residents. Old model, new model. Resident overnight coverage, or attendings in house reading the emergency cases. Dr. Bruno lays out the options as sink or swim.

50% of radiology residency programs are now estimated to have attending overnight coverage. The main arguments have not changed much over the years:

#1: Inaccurate resident interpretations. But, major errors by residents are unusual, less than 1%. Errors that require immediate change in patient management are extremely uncommon. The authors estimate this more severe error rate as about 1 in 10,000.

#2: Quality and safety: Is it safe for residents to interpret a complex case? Training programs use the double reading model. Residents first interpret the case, then the attending. Double reading allows the attending to look for more complex findings; the obvious pneumonia in the left lung is already reported. What about the apical pleural thickening on the right side that represents a carcinoma? Dr. Bruno presents data: double reading with a resident followed by an attending versus attending alone. Twelve times fewer reports were amended with the double reading model.

#3: Training missions. Our patients require the best possible care. Does this mean a moral responsibility to have the attending physician present at all time? What about our moral responsibility to produce the best next generation radiologist? Independent thinking by residents overnight may contribute to the training mission. A survey of residents in 2016 showed 38% said attending coverage overnight had a negative impact on their training. But not all residents agree. Another survey indicated an attending in-house reduced their anxiety and their stress.

#4: Cost: Does your hospital have enough staff available to provide overnight coverage? Does attending coverage overnight simply increase cost with little benefit to patient care?

Summary: There is evidence that major errors by residents are very rare. The residents are better than ever at reading CT and MRI. However, the reason we can have a second-year radiology resident overnight is probably not so complicated. There simply are not that many radiology findings that are immediately life threatening. A large pulmonary embolus on CT is easily seen by a first-year resident. But a subsegmental PE could be missed. But for such a tiny PE, the risk of treatment could be greater than the risk of the small PE. The unrecognized tension pneumothorax does not occur that often. In my 4 years overnight as a resident at Johns Hopkins, I recall one finding that was life threatening and that was not suspected at all by the emergency physician. That was a bowel perforation into the retroperitoneum. The patient had back pain, and a lumbar spine film was ordered. The ED physician saw no spine abnormality and sent the patient home immediately, without even consulting radiology. We got the patient back in a hurry, but the patient was quite stable. On the other hand, Shock Trauma hospital is one of the most famous trauma centers in the world, only about 3 miles away from Johns Hopkins. They have a much higher probability of multi-compartment trauma, very complex. Attending radiologists are in house 24-7.

Dr. Carolyn Meltzer is the chair of Radiology at Emory. In her commentary, she notes that fatigue, stress, and burnout need to be addressed in all of our staff members. What is the culture of your institution? If there are only residents in the emergency room, then residents overnight in radiology may make sense. Dr. Meltzer argues for flexibility on the approach of overnight resident coverage – there should be onsite attending coverage in some centers and graded responsibility for the residents – a combination of junior and senior residents. She also concludes, that in a complex tertiary care hospital or major trauma center, solo resident coverage is not trainee-centered nor patient-centered. I would have to agree.

That concludes this week's articles. I hope these podcasts were helpful to you. Until next time, this is Dr. David Bluemke for the journal *Radiology*. I hope you have a good rest of your week.